Porphyria

By

Dr. Marwa Ali

Lecturer of Medical Biochemistry

Ain Shams university

INTENDED LEARNING OBJECTIVES (ILOs)

By the end of this lecture the student will be able to:

1. **Outline different types of Porphyria**
2. **Correlate biochemical basis of porphyria with its clinical manifestations**

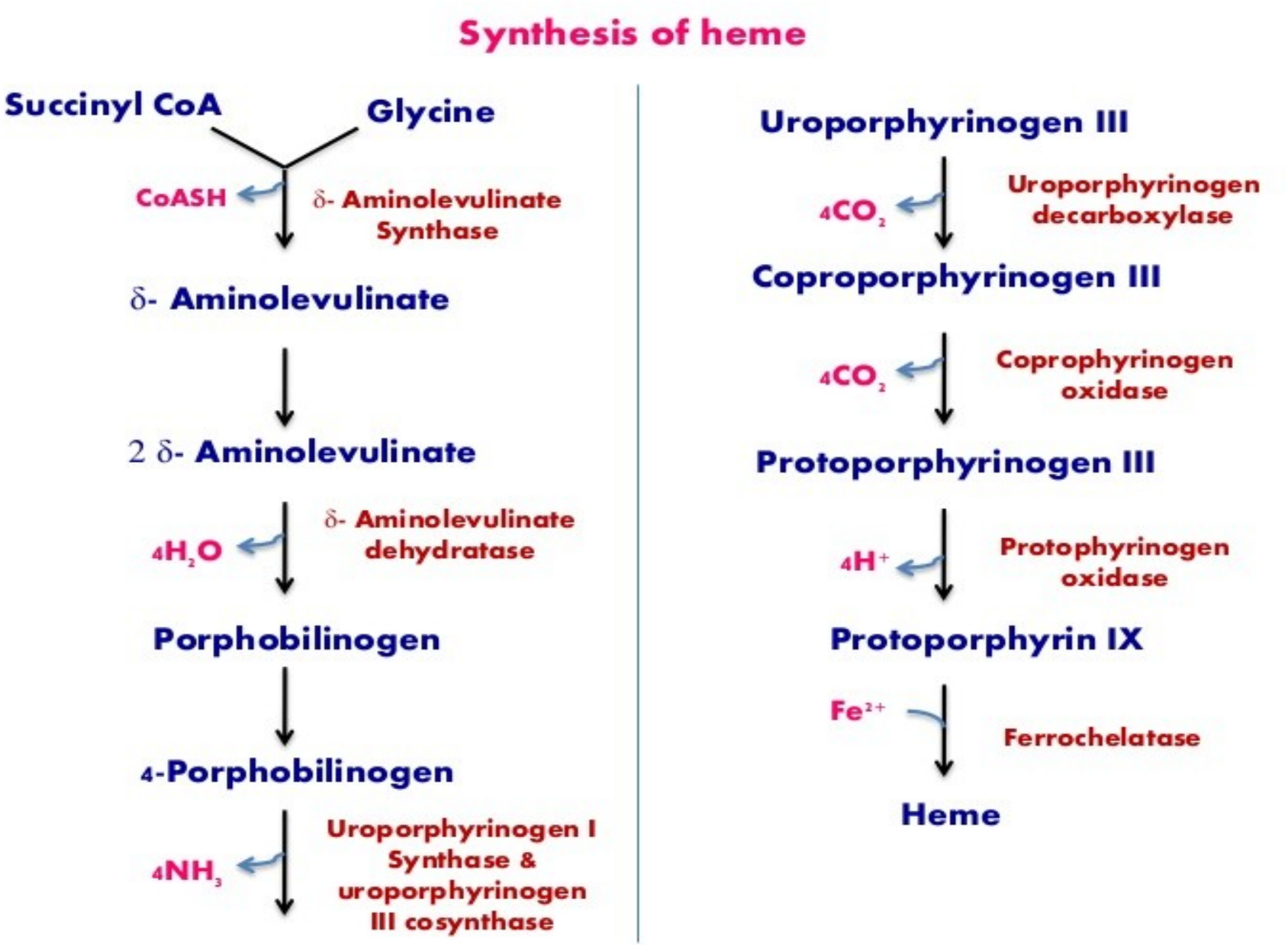
Outlines

Clinical Disorders of Heme Synthesis

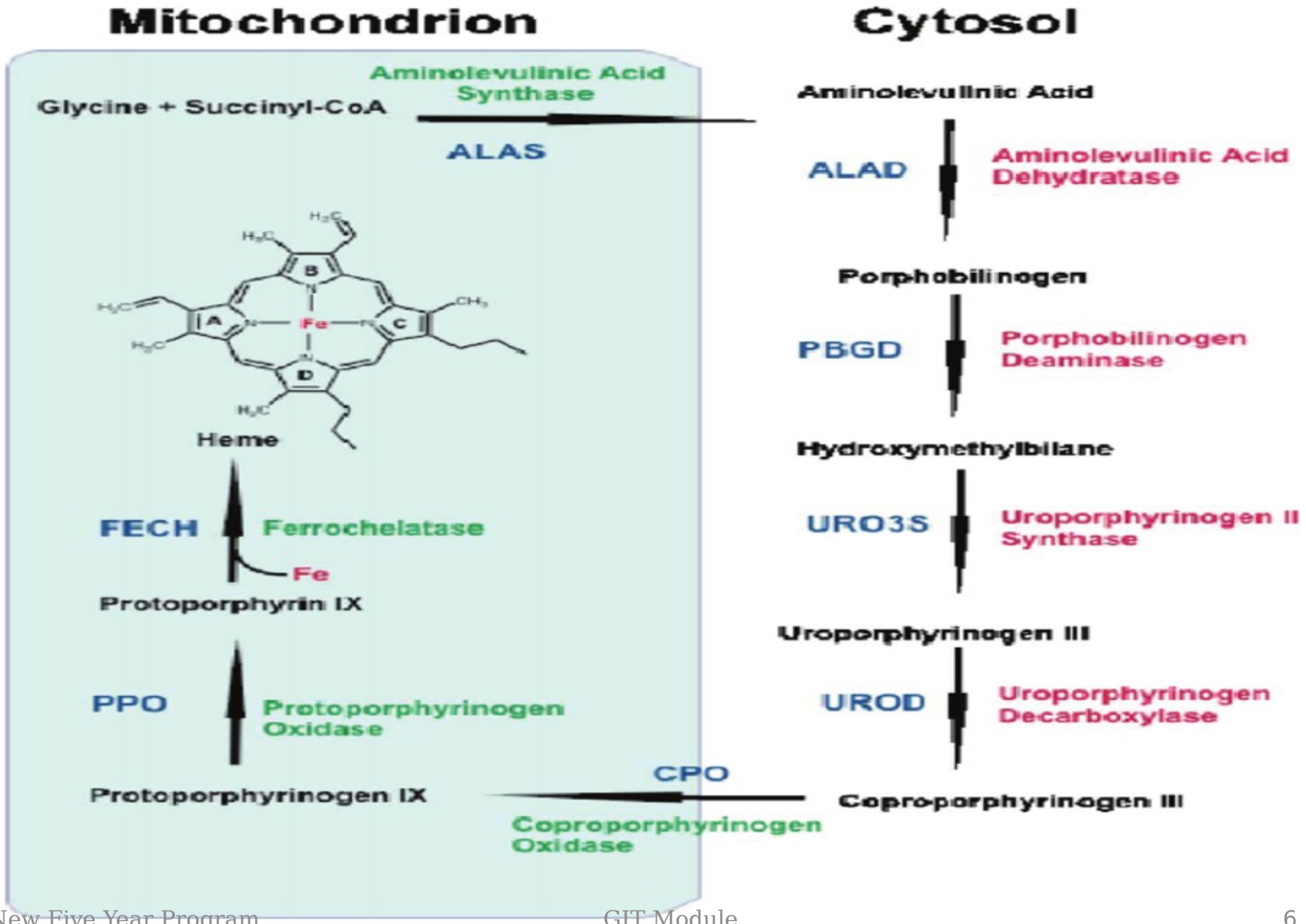
What is Porphyria


Let's
Revise

Overall reactions of heme biosynthesis



Overall reactions of heme biosynthesis



Clinical Disorders of Heme Synthesis

1. Lead Poisoning

Due to high exposure to: Lead paints, batteries and water lead pipes.

:Lead inhibits 2 enzymes

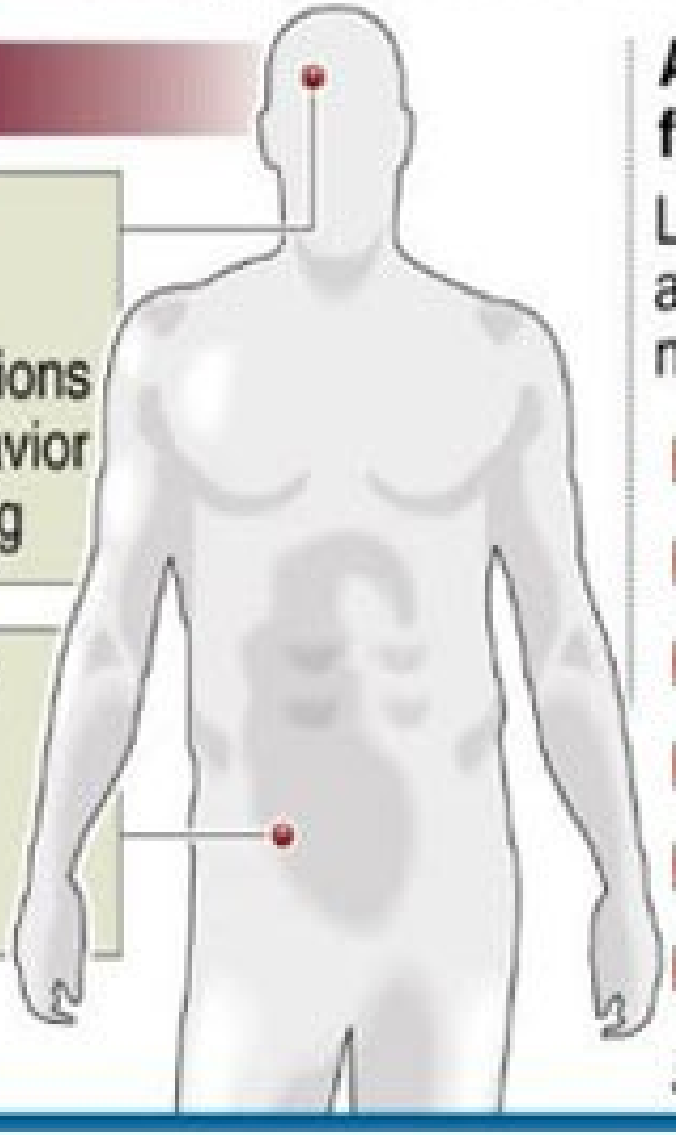
ALA dehydratase & Ferrochelatase

ALA and protoporphyrin accumulate in urine

Elevation in ALA and anemia

Lead poisoning

Lead buildup in the body causes serious health problems



Symptoms

- Headaches
- Irritability
- Reduced sensations
- Aggressive behavior
- Difficulty sleeping

- Abdominal pain
- Poor appetite
- Constipation
- Anemia

Additional complications for children:

Lead is more harmful to children as it can affect developing nerves and brains

- Loss of developmental skills
- Behavior, attention problems
- Hearing loss
- Kidney damage
- Reduced IQ
- Slowed body growth

AFP

Source: MedlinePlus/Mayo Clinic

What is Porphyria

Porphyria

vampire disease

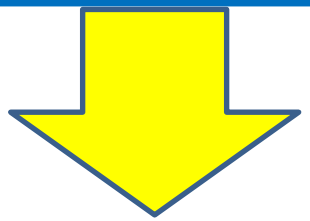
2. Porphyrias

Porphyrias are rare, inherited (or occasionally acquired in lead poisoning) defects in heme synthesis, resulting in the accumulation and increased excretion of porphyrins or porphyrin precursors

2. Porphyrias

Porphyria" refers to the red-blue color caused by pigment-like porphyrins in the urine of patients with defects in heme synthesis

The porphyrias are classified :as



1-Erythropoietic

Hepatic-2

Depending on whether the enzyme deficiency occurs in the erythropoietic cells of the bone marrow or in the liver

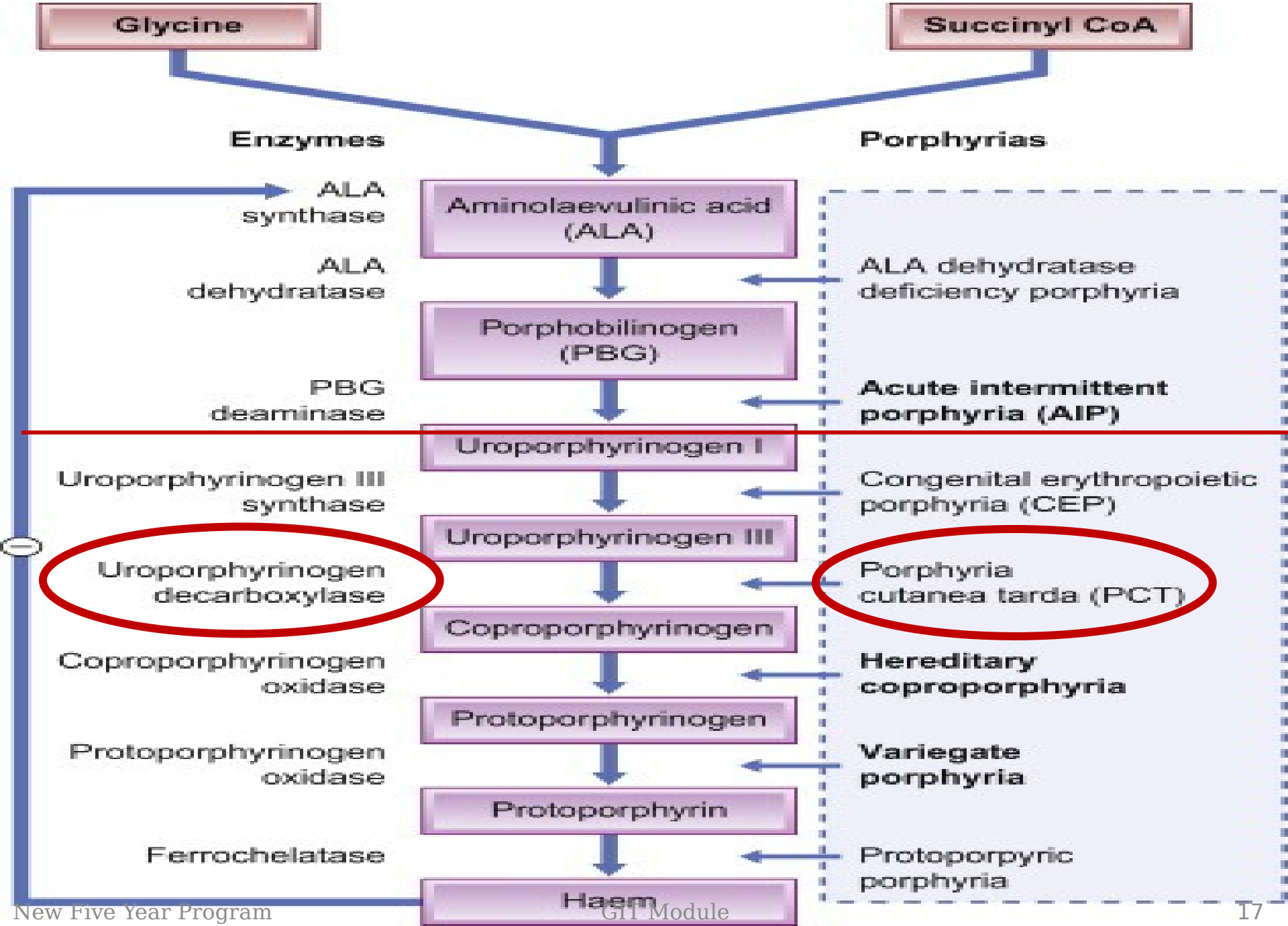
Clinical :manifestations

If the enzyme defect prior to the formation of porphyrinogens (tetrapyrroles)

Abdominal and neuropsychiatric signs

If the enzyme defects after the formation porphyrinogens

Photosensitivity
skin itches, burns and) pruritus on exposure to (visible light

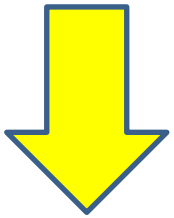

Glycine
Succinyl CoA
Enzymes
Porphyrias
ALA synthase
Aminolaevulinic acid (ALA)
ALA dehydratase
ALA dehydratase deficiency porphyria
Porphobilinogen (PBG)
PBG deaminase
Acute intermittent porphyria (AIP)
Uroporphyrinogen I
Uroporphyrinogen III synthase
Congenital erythropoietic porphyria (CEP)
Uroporphyrinogen III
Uroporphyrinogen decarboxylase
Porphyria cutanea tarda (PCT)
Coproporphyrinogen
Coproporphyrinogen oxidase
Hereditary coproporphyria
Protoporphyrinogen
Protoporphyrinogen oxidase
Variegate porphyria
Protoporphyrin
Ferrochelatase
Protoporpyric porphyria
Haem

Note: Photosenstivity is a result of the oxidation of colorless porphyrinogens to colored porphyrins, that participate in the formation of superoxide radicals .from oxygen

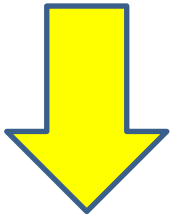
These reactive oxygen species can oxidatively damage membranes and cause the release of destructive enzymes from .lysosomes

Clinical :manifestations

One common feature of the porphyrias is a decreased synthesis of heme



Increase in the synthesis of ALAS1 (derepression)



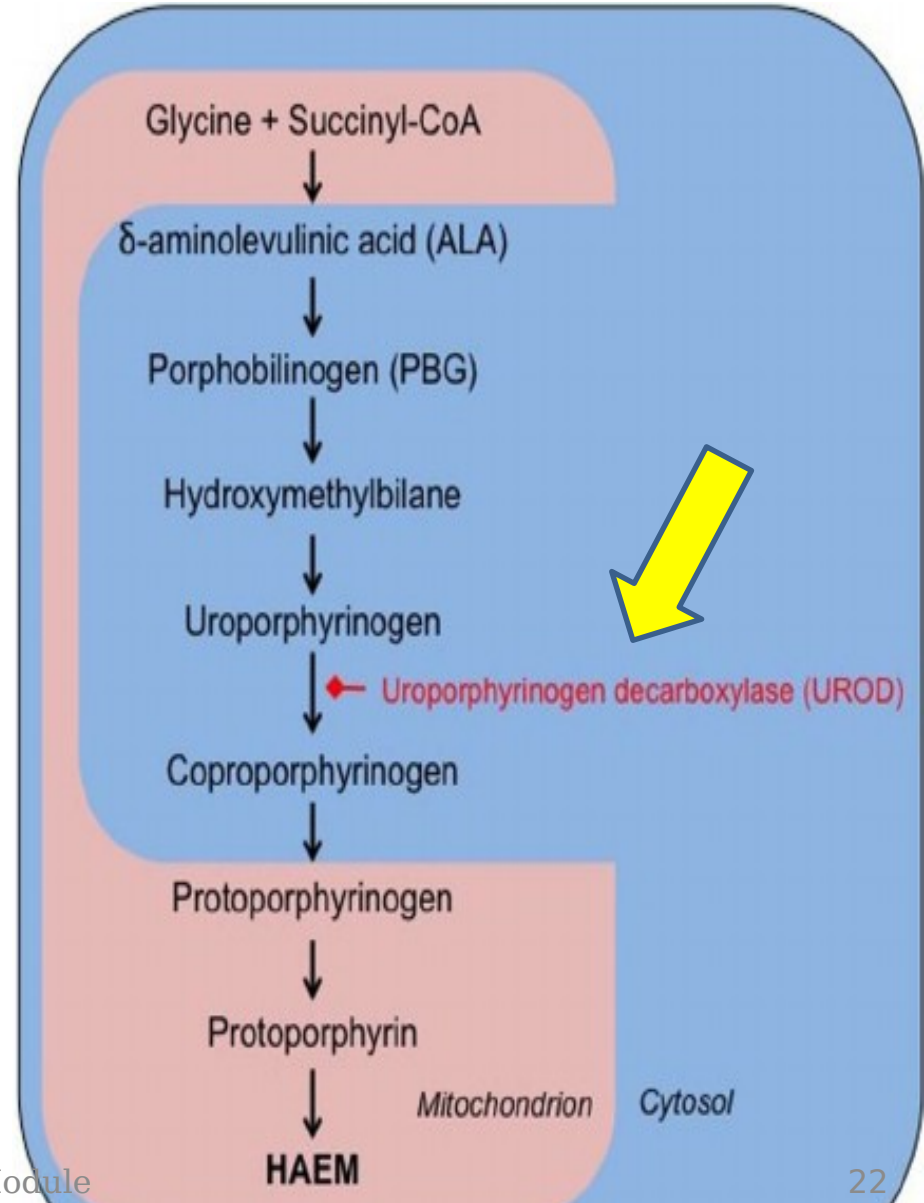
Increased synthesis and accumulation of toxic intermediates that occur prior to the genetic block

Porphyria Cutanea Tarda

Porphyria cutanea tarda

It is the most common porphyria

It occurs due to deficiency in uroporphyrinogen decarboxylase enzyme



Porphyria cutanea tarda

Clinical onset is during the fourth or fifth decade of life

Porphyrin accumulation leads to cutaneous symptoms and red to brown urine in natural light

Note: Symptoms of the acute hepatic porphyrias often precipitated by drugs that cause induction of cytochrome P450 e.g. .steroids , alcohol, Phenobarbital These drugs are contraindicated .for porphyria patients

?WHY

?WHY

Intake of drugs as barbiturates or ethanol

Induce the synthesis of the heme containing .cytochrome P450 required for their metabolism

Decrease heme level in liver cells

Increase synthesis of ALAS

More increase of porphyrins & exacerbation of symptoms

Treatment

No curable treatment, only medical support during acute attacks and symptomatic treatment for pain and vomiting

Treatment

1. **Intravenous injection of hemin and glucose to decreases the synthesis of ALAS1.**
2. **Avoidance of precipitating drugs.**
3. **Protection from sunlight.**
4. **Anti-oxidants: vitamin A (β-carotene) & Vit E in cases of photosensitivity.**

MCQ

Biochemical basis of precipitation -1 :of porphyria by barbiturates is

A. Repression of ALA synthase

B. Derepression of ALA synthase

C. Rerepression of ALA synthase

D. MiRNA mediated

MCQ

Most common porphyria is due to -2 :deficiency of

A. PBG deaminase

B. Uroporphyrinogen decarboxylase

C. Ferrocheletase

D. Coproporphyrinogen oxidase

E. ALA synthase

Summary

- **Lead poisoning is due to high exposure to:**

  Lead paints, batteries and water lead pipes.

- **Porphyria" refers to the red-blue color caused by pigment-like porphyrins in the urine of patients with defects in heme synthesis**

- **Porphyria cutanea tarda occurs due to deficiency in uroporphyrinogen decarboxylase enzyme**

Thank you

Marwa Al